OIPE JC18
AUG 15 2005
PATENT & TRADEMARK OFFICE

Attorney Docket No. 021706-000420US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 7565
Albert Zorko Abram, et al.	Examiner: Mina Haghighatian
Application No.: 10/763,379	Technology Center/Art Unit: 1616
Filed: January 23, 2004	DECLARATION UNDER
For: PHARMACEUTICAL FOAM	37 C.F.R. § 1.131
Customer No.: 20350	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, the undersigned inventors, declare as follows:

1. We are the only inventors of the invention claimed in the above-captioned patent application.

2. We understand that in an Office Action, certain of the claims have been rejected as allegedly being obvious over U.S. Patent Publication No. 2004/0043946 to Popp, which claims priority to U.S. Provisional Patent Application No. 60/407,285, filed on September 3, 2005.

3. We conceived the invention disclosed and claimed in the relevant claims of the instant application prior to September 3, 2002 and were diligent in reducing to practice the same before such date.

4. Enclosed as Exhibit A are pages 58-63 of a joint inventor's laboratory notebook, provided to illustrate our diligence in reducing the invention claimed in the above-identified application to practice. Pages 58-63 of Exhibit A demonstrate our conception and reduction to practice of a topical delivery composition in a pressurized container comprising up to 15% of a pharmaceutically active compound, about 83%-97.9% of a quick-breaking foaming agent comprised of a C_1-C_6 alcohol, a

C_{14}-C_{22} alcohol, water, and a surfactant, and about 2%-7% of a propellant, wherein the pH adjusting agent is an acid or a base.

5. The dates on the pages of the enclosed Exhibit A have been redacted. All such redacted dates are prior to September 3, 2002.

6. We further declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Date: 9 August, 2005

Albert Zorko Abram

Date: 9 Aug 2005

Barry Thomas Hunt

60548902 v1

OIPE JCIAS
AUG 15 2005
PATENT & TRADEMARK OFFICE

E130/15

Date Redacted

Clinda mousse - pH changes

SP008

Aim

1. **Purpose**

This protocol will monitor the pH changes of clindamycin phosphate 1% foam formulas adjusted to 5 different pHs at 25°C. The pH of the water phase and of the finished product will be monitored. The purposes of this study are to (a) redefine the correlation between pH of water phase and pH of finished product, and (b) track changes in these pH values over a 6 month period.

2. **Test Materials**

The base formula and variations are shown below.

Component	Grade	% w/w
Ethanol, dehydrated	USP	58.21
Stearyl alcohol	NF	0.53
Cetyl alcohol	NF	1.16
Polysorbate 60	NF	0.42
Propylene glycol	USP	2.11
Purified water	USP	to 100% (approx 36%)
Clindamycin Phosphate (804 mg/g)	USP	1.246

Potassium hydroxide 10% solution	NF	qs to required pH. 4.50, 4.55, 4.70, 4.85, 4.90

Each can will be filled with 19.0 +/- 0.4g water phase and 31.5 +/- 0.4g ethanol phase. Cans will be crimped and gassed with 2.66 +/- 0.25g P70.

Make a bulk ethanol phase, common to all formulations, and a bulk Clinda/water phase - divided into sub-batches for pH adjustment.

5 pHs x 8 cans @ 53g/can = 2120g, plus 5 x 100g base = 2620g. Make enough for 3000g.

BEST AVAILABLE COPY

E130/15 contd

Date Redacted

Clinda mousse pH changes SP008

E130/15/1 F130/15/1

Item	%	Ingredient	g/3000g
1	58.21	Ethanol 96 100 HG	1746
2	0.53	Dehydag wax 14	15.9
3	1.16	" " 16	34.8
4	0.42	Crillet 3	12.6
5	2.11	Prop. glycol	63.3
	62.43		1873
6	34.00	Water, purified	1020
7	1.246	Clinda. phosphate	37.4
	35.246		1057

Total 97.676

KOH 10% qs to pH

water → 100%

Slightly less water is being used at Item 6 to allow for variable KOH addition. Then make up to full weight with water.

From previous studies (E123/24, p 48) the amount of 1% KOH used was 1 - 2g per 70g of water phase.

Water phase divided into lots of 210g. Full weight of water phase (incl. KOH) is (100 - 62.43) = 37.57 x 30 = 1127g ÷ 5 = 225g. So each lot of 210g is adjusted to pH with 10% KOH then made up to 225g with water.

BEST AVAILABLE COPY

F130/15 Cream

Soltec Research Pty Ltd. Manufacturing Batch Record

(Samples only)

Product Name: **SP008** — Clindamycin Phosphate Mousse pH testing

Formulation No: F130/15
Batch No: E130/15
Date: [redacted]
Batch Size: [redacted] 3000 grams

Item No.	% w/w	Ingredient	Lot #	Theoretical Mass Weighed.	Actual Mass weighed	Weighed By	Checked By
1	58.21	Ethanol 100HG	21280	1746.300	1751.6	[redacted]	[redacted]
2	0.42	Crillet 3	98437	12.600	12.77	[redacted]	[redacted]
3	0.53	Dehydag wax 18	13347	15.900	13.89	[redacted]	[redacted]
4	1.16	Dehydag wax 16	13348	34.800	34.83	[redacted]	[redacted]
5	2.11	Propylene glycol	21097	63.300	63.62	[redacted]	[redacted]
				8129			
6	34.00	Purified water	—	1020.000	1020.33	[redacted]	[redacted]
7	1.25	Clindamycin phosphate	20086	37.380	37.50	[redacted]	[redacted]
8	qs	Potassium hydroxide 10% soln					
9	qs	Purified water					
	97.676	TOTAL		2930.280	(No propellant)		

1872.9
615.6
2488
Actual = 2497g
34
1463.46
44.13
1020.33

Method:
Ethanol phase:
Dissolve 2 - 5 in ethanol.
Water phase:
Add 7 to 6 and mix till dissolved
Prepare a 10%w/w KOH solution and adjust water phase as reqd.
Add remaining purified water to 100%.

Fill weights: (50.5g base)
Ethanol ph 31.5 +/- 0.40g
Water ph 19.0 +/- 0.40g
Propellant 2.66 +/- 0.25g

[redacted] Date Redacted

[redacted] Date Redacted

60

BEST AVAILABLE COPY

E130/15 contd

Date Redacted

Clinda mousse pH SP008

Take 211 g ± 1 g of water phase, and add 10% KOH soln (10% w/w 20045 in water) to achieve pH, ± 0.01 unit. Then → 225g ± 1g + re-check pH

pH meter calibrated at 25° ± 2°C, sample solutions at 25° ± 2°C.

19.0 ± 0.4 g of ~~bath~~ soln water phase into 8 7 aerosol cans (35x125 mm Exal), add 31.5 ± 0.4g of ethanol phase, then crimp. Gas with 2.66 ± 0.25 g 170. Remaining water phase into 120 ml glass jar.

All samples stored at 25°C. 1 sample of water phase + ethanol ph for pH measurement (not aerosol).

g 10% KOH to in 211g	Ref. no.		pH nominal	pH actual	App. pH base
0.41g	E130/15	2	4.50	4.49	
0.46g	–	3	4.55	4.57	
0.56	–	4	4.70	4.70	
0.78g	–	5	4.85	4.85	
0.82g	–	6	4.90	4.90	

re-checked pH 4.0 buffer after each ~~addition~~ batch. (Initial pH 3.21)

For 2nd batch onwards the water was added to 224g immediately (because such a small amt of KOH is used)

Checked both pH 4 & 7 at end, both within 0.02

Recalibrate pH meter at 40°C + check pH of the 5 mixed aq/eth phases at 40°C

BEST AVAILABLE COPY

E130/15 contd [redacted]

	App. pH c. corr	
E130/15/2	4.85	
3	4.92	pH4 now = 3.99
4	5.03	
5	5.15	
6	5.20	pH4 now = 4.00
		pH7 now = 7.02

[redacted]

The above jars placed at 25°C on 30/10.
Cans filled yesterday were gassed today with 2.66 ±0.25g P70.
Cans waterbathed labelled & weighed. Weights are to check on gas loss - not for formal study.

Into 25°C today.

Sample 7 label used

For Laboratory Evaluation Only
Not for Human Use
Clindamycin Mousse pH testing SP008
Time point: 1 2 4 weeks 2 3 6 months
Storage temperature: 25°C
E130/15/8
SOLTEC RESEARCH Pty. Ltd.

[redacted]

BEST AVAILABLE COPY

E130/15 contd

Date Redacted

Climate SB008 - 1 week

(Actually 8 days)

Check pH ↑ to 5 years from 25°C.

E130/15/2	~~4.81~~ 4.43	
3	4.54	
4	4.66	
5	4.81	
6	4.87	

pH 4 max = 3.98, adj → 4.00

Recal. @ 40°C

App pH @ 40°C =

2	4.84
3	4.91
4	5.03
5	5.16
6	5.21

pH 4 max = 3.99, adj → 4.00

pH 4 max = 4.00

Date Redacted

to p70

BEST AVAILABLE COPY